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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,252	04/12/2001	Regine Helibronn	100564-00044	5869

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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	11

DATE MAILED: 11/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,252	HELIBRONN, REGINE	
	Examiner	Art Unit	
	Gerald G Leffers Jr.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-13 and 15-30* is/are pending in the application.

4a) Of the above claim(s) *28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-13,15-27,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Receipt is acknowledged of applicant's election with traverse in Paper No. 8, filed 8/23/02, of Group I (claims 1-13, 16-17). Applicant's response argued that the limitation of inserting the AAV rep and cap genes into the genome of the HSV virus is not taught by the Conway et al (1997) reference cited by the examiner in making the restriction. As there is support for this limitation in the specification as filed and as applicants' assertion is correct for Groups I-V, the restriction requirement has been withdrawn for Groups I-V and all claims therein have been rejoined for examination. Claim 28 (Group VI) does not comprise the special technical feature of the elected claims (i.e. the hybrid HSV/AAV virus) and is therefore not rejoined for prosecution.

Receipt is acknowledged of an amendment, filed 9/10/02 as Paper No. 10, in which applicant cancelled claims 1 and 14, submitted new claims (30-31) and amended several claims (claims 2-4, 7-10, 15-16, 18 and 23). However, it is noted that there has been no claim 29 filed in this application to date. **Therefore, newly submitted claims 30 & 31 have been renumbered as claims 29 & 30, respectively (Rule 126).** Thus, claims 2-13 and 15-30 are pending in the instant application, with claim 28 being withdrawn from consideration as being directed to a nonelected invention.

Claim Objections

Claims 2-13 and 15-27 are objected to because of the following informalities: the dependency of each claim appears to be incorrect because the newly added claims upon which

the remaining claims are dependent (i.e. added claims 30-31) have been renumbered (see above). It would be remedial to amend the claims to have the appropriate dependency on claims 29 and 30. Appropriate correction is required.

Information Disclosure Statement

Receipt is acknowledged of an IDS filed 8 January 2001 as Paper No. 5. The signed and initialed PTO Form 1449 has been mailed with this action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-13 and 15-27 and 29-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-13, 16-27 are vague and indefinite in that the claims all recite in some form the limitation of the "recombinant herpesvirus of claim 30". As noted above, claim 30 has been renumbered as claim 29 under Rule 126. It would be remedial to amend these claims to be dependent on claim 29.

Claim 2 is vague and indefinite in that the metes and bounds of the phrase "...which does not exhibit any reversion to the wild type..." are unclear. The phrase is unclear as to under what conditions the rate of reversion is to be measured, what the "wild type" is supposed to be (e.g. AAV or HSV, etc.) or for what period of time reversion is supposed to be measured in order to

satisfy the claim limitation of not exhibiting reversion to wild type. It would be remedial to amend the claim language to clearly indicate these parameters.

Claim 6 is vague and indefinite in that the claim recites a recombinant hybrid vector comprising AAV rep and cap genes and then specifies that the hybrid vector is a "HSV-1 mutant 1802", when the 1802 mutant is known in the art as not being a hybrid vector. Upon reading the specification (e.g. page 7, line 25), it appears the phrase is meant to specify that the AAV rep and cap genes have been integrated into the genome of the HSV-1 mutant 1802.

Claim 7 is vague and indefinite in that the metes and bounds of the phrase "...a mutant which is completely or partially replication-deficient..." are unclear. The specification does not clearly define "completely" or "partially" with regard to replication deficiency. Where does one limitation begin and the other end? Under what conditions is the hybrid virus of the invention completely or partially replication-deficient?

Claim 10 is vague and indefinite in that the metes and bounds of the term "stably integrated" are unclear. This term does not appear to the clearly described in the specification. Under what conditions and for how long does the integrant have to be "stable"? How "stable" does the integrant have to be in order to satisfy the limitation? Does the limitation mean the integrant can never be removed from the viral genome by any means? It would be remedial to amend the claim language to more clearly indicate what is meant by a "stable" integrant.

Claims 12-13 and 21-22 are vague and indefinite in that the metes and bounds of the phrase "...wherein use is made of..." a virus. As the claims are currently written, the intended use of the recited virus is unclear. Is it used somehow in the construction of the hybrid

HSV/AAV virus or is it used for some other purpose? It would be remedial to amend the claim language to clearly indicate how the recited virus is used in the claimed process.

Claim 18 is vague and indefinite in that the metes and bounds of the words "based on" are unclear. To what degree does a viral vector have to be in common with an AAV virus for it to be "based on" the AAV virus? Would a sequence of two nucleotides in common satisfy the limitation? Would a promoter obtained from an AAV genome substituted into an adenoviral vector satisfy the limitation? It would be remedial to amend the claim language to more specifically claim the viral vector of step (a).

Claim 24 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "the vector" in the claim upon which claim 24 is dependent.

Claims 29-30 are vague and indefinite in that the metes and bounds of the phrase "...a rep and a cap gene derived from ..." are unclear. It is unclear the nature and number of steps required in order to obtain a "derivative" of a rep or cap gene. It would be remedial to amend the claim language by substituting the word "obtained" for the word "derived" in these claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2-5, 7-13, 15-27 and 29-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Dong et al (WO 95/06743; reference AG on IDS #5 submitted by applicant; see the entire reference).

Dong et al teach the construction of helper viruses for production of rAAV which comprise genes essential for AAV replication (e.g. Abstract). Dong et al teach that the helper viruses of their invention can be obtained from adenovirus or one of several different types of viruses classified in a general class of "herpesvirus", including HSV (e.g. page 6, lines 16-28). Dong et al teach that these helper viruses can either be replication competent (i.e. comprising viral packaging and origin of replication sequences) or replication defective (e.g. page 15, lines 19-29). Dong et al specifically teach that the herpesvirus helper viruses of their invention will, generally speaking, comprise one or more of the AAV rep, lip and cap genes (e.g. page 7, lines 8-20). Dong et al teach that the essential or non-essential genes from the helper virus genome have been deleted (e.g. page 7, lines 21-32). Dong et al teach that the helper viruses of their invention can promote expression of the essential AAV genes with either natural AAV promoters (e.g. p5 from AAV) or heterologous promoters (e.g. IE from CMV, retroviral LTR elements) (page 8, lines 20-27; page 9, lines 4-14). The reference teaches that the nature of the herpes family virus is not believed to be crucial to the successful practice of the invention (e.g. herpes simplex virus, cytomegalovirus, etc.) (page 32, line 20 to page 33, line 9). Dong et al teach a prophetic example for insertion of AAV rep, lip and/or cap sequences into the genome of HSV feature the HSV vector R7020. R7020 features deletion of approximately 700 bp from the domain of the thymidine kinase gene and all of the sequences from the 3' end of the IE63 gene (a27) to the a4 gene in the reiterated sequences of the S component of the HSV genome. Dong et

al teach that the rep-lip-cap sequences can be inserted in, at least, either of two positions including the site between the inserted tk gene and the HSV-2 DNA sequences and the site of the deletion of the natural tk gene (e.g. Example VI(1), page 44).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.
Examiner
Art Unit 1636

Ggl
November 20, 2002